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EXAMINER	
MINNIFIELD, NITA M	

ART UNIT	PAPER NUMBER
1645	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/816,220	DAVIS ET AL.	
	Examiner	Art Unit	
	N. M. Minnifield	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *5/14/07; 7/02/07*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 62-95* is/are pending in the application.

4a) Of the above claim(s) *62,63,65,68,76,86-88,90 and 92-95* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,64,66,67,69-75,77-81, 83-85,89 and 91* is/are rejected.

7)☒ Claim(s) *82* is/are objected to.

8)☒ Claim(s) *62,63,65,68,76,86-88,90 and 92-95* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *01 April 2004* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/28/05; 6/23/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Sequence Requirements

1. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 C.F.R. §§ 1.821-1.825 for the reason(s) set forth: sequences are recited on page 39, line 23; page 40, line 26 and page 41, line 23 however there are no sequence identifiers for these recited sequences. Applicants are encouraged to review the entire specification for sequence compliance.

Full compliance with the sequence rules is required in response to this office action. A complete response to this office action should include both compliance with the sequence rules and a response to the Non-Final Office Action set forth below. Failure to fully comply with ***both*** these requirements in the time period set forth in this office action will be held non-responsive.

2. Applicant's election of species (a) a disease/condition/infection that is herpes simplex virus infection as recited in claim 70; (b) an anti-viral agent that is acyclovir as recited in claim 75; (c) an immune response that is an innate immune response as recited in claim 91; and (d) an immunostimulatory nucleic acid having the nucleotide sequence of SEQ ID NO: 150 as recited in claim 82 in the reply filed on May 14, 2007 is acknowledged. These elections embrace at least claims 1, 64, 66, 67, 69-75, 77-85, 89 and 91. Because applicant did not distinctly and

specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

3. Claims 62, 63, 65, 68, 76, 86-88, 90 and 92-95 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on May 14, 2007.

4. The use of trademark has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

5. The disclosure is objected to because of the following informalities: page 36, line 12 recites "evin", should be "even". There are two occurrences of Table 1, see pages 55 and 76. Appropriate correction is required.

6. The informal drawings are not of sufficient quality to permit examination. Accordingly, replacement drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to this Office action. The replacement sheet(s) should be labeled "Replacement Sheet" in the page header (as per 37 CFR 1.84(c)) so as not to obstruct any portion of the drawing figures. If the changes are not accepted by the

examiner, the applicant will be notified and informed of any required corrective action in the next Office action.

Further, the figure description should describe the various symbols in the figures (all three figures).

7. Claim 84 is objected to because of the following informalities: the claim should recite "oral delivery" instead of "oral deliver". Appropriate correction is required.

8. The attempt to incorporate subject matter into this application by reference to patent applications and/or PCT applications (see pages 4, 38 and 54) is ineffective because an application as filed must be complete in itself in order to comply with 35 U.S.C. 112. Material nevertheless may be incorporated by reference, Ex parte Schwarze, 151 USPQ 426 (Bd. Ape. 1966). An application for a patent when filed may incorporate "essential material" by reference to (1) a U.S. patent, (2) a U.S. patent application publication, or (3) a pending U.S. application, subject to the conditions set forth below. "Essential material" is defined as that which is necessary to (1) describe the claimed invention, (2) provide an enabling disclosure of the claimed invention, or (3) describe the best mode (35 U.S.C. 112). In any application which is to issue as a U.S. patent, essential material may not be incorporated by reference to (1) patents or applications published by foreign countries or a regional patent office, (2) non-patent publications, (3) a U.S. patent or application which itself incorporates "essential material" by reference, or (4) a foreign application.

It is noted that patent applications recited on page 4 describe essential material, the various classes of immunostimulatory nucleic acids that are recited in claim 89. It is also noted that page 4 only recites "incorporated herein in their entirety". Some of the patent applications have been abandoned and there is no corresponding PG Publication.

The incorporation by reference will not be effective until correction is made to comply with 37 CFR 1.57(b), (c), or (d). If the incorporated material is relied upon to meet any outstanding objection, rejection, or other requirement imposed by the Office, the correction must be made within any time period set by the Office for responding to the objection, rejection, or other requirement for the incorporation to be effective. Compliance will not be held in abeyance with respect to responding to the objection, rejection, or other requirement for the incorporation to be effective. In no case may the correction be made later than the close of prosecution as defined in 37 CFR 1.114(b), or abandonment of the application, whichever occurs earlier. Any correction inserting material by amendment that was previously incorporated by reference must be accompanied by a statement that the material being inserted is the material incorporated by reference and the amendment contains no new matter. 37 CFR 1.57(f).

9. Claims 1, 64, 66, 67, 69-75, 77-81, 83-85, 89 and 91 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant

art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The pending claims (for example claim 1) are a method for inducing an immune response comprising topically administering to a subject an oil-water emulsion and an immunostimulatory nucleic acid in an amount effective to induce an immune response. The claims do not recite the structure of the immunostimulatory nucleic acid. Dependent claim 64 defines that the immunostimulatory nucleic acid is a CpG immunostimulatory nucleic acid.

A review of the specification discloses a list of immunostimulatory nucleic acids that could be used in the claimed invention. The claims do not recite the structure for the immunostimulatory nucleic acid, save claim 64 that only defines a C and G. The claims only indicate that it is a nucleic acid. The claims do not set forth a structure for the claimed immunostimulatory nucleic acid molecule. The specification does not teach an immunostimulatory nucleic acid molecule having only 2 nucleic acids.

MPEP § 2163.02 states, "[a]n objective standard for determining compliance with the written description requirement is, 'does the description clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed' ". The courts have decided: The purpose of the "written description" requirement is broader than to merely explain how to "make and use"; the applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the "written description" inquiry, whatever is now claimed. See Vas-Cath, Inc. v. Mahurkar, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Federal Circuit, 1991). Furthermore, the written description provision of 35 USC

§ 112 is severable from its enablement provision; and adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. The Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, paragraph 1, "Written Description" Requirement (66 FR 1099-1111, January 5, 2001) state, "[p]ossession may be shown in a variety of ways including description of an actual reduction to practice, or by showing the invention was 'ready for patenting' such as by disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention" (Id. at 1104). Moreover, because the claims encompass a genus of an immunostimulatory nucleic acid molecule, an adequate written description of the claimed invention must include sufficient description of at least a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics sufficient to show that Applicant was in possession of the claimed genus. However, factual evidence of an actual reduction to practice has not been disclosed by Applicant in the specification; nor has Applicant shown the invention was "ready for patenting" by disclosure of drawings or structural chemical formulas that show that the invention was complete; nor has Applicant described distinguishing identifying characteristics sufficient to show that Applicant were in possession of the claimed invention at the time the application was filed.

The Guidelines further state, "[f]or inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species

cannot be achieved by disclosing only one species within the genus" (Id. at 1106); accordingly, it follows that an adequate written description of a genus cannot be achieved in the absence of a disclosure of at least one species within the genus. Therefore, absent a detailed and particular description of a representative number, or at least a substantial number of the members of the genus of compositions, the skilled artisan could not immediately recognize or distinguish members of the claimed antigenic compositions. In view of the above, the instant specification fails to meet the written description requirement as set forth under 35 U.S.C. 112, first paragraph.

A lack of adequate written description issue also arises if the knowledge and level of skill in the art would not permit one skilled in the art to immediately envisage the product claimed from the disclosed process. See, e.g., Fujikawa v. Wattanasin, 93 F.3d 1559, 1571, 39 USPQ2d 1895, 1905 (Fed. Cir. 1996) (a "laundry list" disclosure of every possible moiety does not constitute a written description of every species in a genus because it would not "reasonably lead" those skilled in the art to any particular species); In re Ruschig, 379 F.2d 990, 995, 154 USPQ 118, 123 (CCPA 1967) ("If n-propylamine had been used in making the compound instead of n-butylamine, the compound of claim 13 would have resulted. Appellants submit to us, as they did to the board, an imaginary specific example patterned on specific example 6 by which the above butyl compound is made so that we can see what a simple change would have resulted in a specific supporting disclosure being present in the present specification. The trouble is that there is no such disclosure, easy though it is to imagine it.") (emphasis in original); Purdue Pharma L.P. v. Faulding Inc., 230 F.3d 1320, 1328, 56 USPQ2d 1481,

1487 (Fed. Cir. 2000) ("the specification does not clearly disclose to the skilled artisan that the inventors ... considered the ratio.., to be part of their invention .... There is therefore no force to Purdue's argument that the written description requirement was satisfied because the disclosure revealed a broad invention from which the [later-filed] claims carved out a patentable portion"). A specification may describe an actual reduction to practice by showing that the inventor constructed an embodiment or performed a process that met all the limitations of the claim and determined that the invention would work for its intended purpose. Cooper v. Goldfarb, 154 F.3d 1321, 1327, 47 USPQ2d 1896, 1901 (Fed. Cir. 1998). See also UMC Elecs. Co. v. United States, 816 F.2d 647, 652, 2 USPQ2d 1465, 1468 (Fed: Cir. 1987) ("[T]here cannot be a reduction to practice of the invention without a physical embodiment which includes all limitations of the claim."); Estee Lauder Inc. v. L'Oreal, S.A., 129 F.3d 588, 593, 44 USPQ2d 1610, 1614 (Fed. Cir. 1997) ("[A] reduction to practice does not occur until the inventor has determined that the invention will work for its intended purpose."); Mahurkar v. C.R. Bard, Inc., 79 F.3d 1572, 1578, 38 USPQ2d 1288, 1291 (Fed. Cir. 1996) (determining that the invention will work for its intended purpose may require testing depending on the character of the invention and the problem it solves).

For some biomolecules, examples of identifying characteristics include a sequence, structure, binding affinity, binding specificity, molecular weight, and length. Although structural formulas provide a convenient method of demonstrating possession of specific molecules, other identifying characteristics or combinations of characteristics may demonstrate the requisite possession. >As explained by the Federal Circuit, "(1) examples are not necessary to support the adequacy of a written description; (2) the written description standard may be met

... even where actual reduction to practice of an invention is absent; and (3) there is no per se rule that an adequate written description of an invention that involves a biological macromolecule must contain a recitation of known structure." Falkner v. Inglis, 448 F.3d 1357, 1366, 79 USPQ2d 1001, 1007 (Fed. Cir. 2006). See also Capon v. Eshhar, 418 F.3d at 1358, 76 USPQ2d at 1084 ("The Board erred in holding that the specifications do not meet the written description requirement because they do not reiterate the structure or formula or chemical name for the nucleotide sequences of the claimed chimeric genes" where the genes were novel combinations of known DNA segments.). For example, disclosure of an antigen fully characterized by its structure, formula, chemical name, physical properties, or deposit in a public depository provides an adequate written description of an antibody claimed by its binding affinity to that antigen. Noelle v. Lederman, 355 F.3d1343, 1349, 69 USPQ2d 1508, 1514 (Fed. Cir. 2004) (holding there is a lack of written descriptive support for an antibody defined by its binding affinity to an antigen that itself was not adequately described). Additionally, unique cleavage by particular enzymes, isoelectric points of fragments, detailed restriction enzyme maps, a comparison of enzymatic activities, or antibody cross- reactivity may be sufficient to show possession of the claimed invention to one of skill in the art. See Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966 ("written description" requirement may be satisfied by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that fully set forth the claimed invention"). A definition by function alone "does not suffice" to sufficiently describe a coding sequence "because it is only an indication of what the gene does, rather than what it is." Eli Lilly, 119 F.3 at 1568, 43 USPQ2d at 1406. See also

Fiers, 984 F.2d at 1169-71, 25 USPQ2d at 1605-06 (discussing Amgen Inc. v. Chugai Pharmaceutical Co., 927 F.2d 1200, 18 USPQ2d 1016 (Fed. Cir. 1991)). An adequate written description of a chemical invention also requires a precise definition, such as by structure, formula, chemical name, or physical properties, and not merely a wish or plan for obtaining the chemical invention claimed. See, e.g., Univ. of Rochester v. G.D. Searle & Co., 358 F.3d 916, 927, 69 USPQ2d 1886, 1894-95 (Fed. Cir. 2004) (The patent at issue claimed a method of selectively inhibiting PGHS-2 activity by administering a non-steroidal compound that selectively inhibits activity of the PGHS-2 gene product, however the patent did not disclose any compounds that can be used in the claimed methods. While there was a description of assays for screening compounds to identify those that inhibit the expression or activity of the PGHS-2 gene product, there was no disclosure of which peptides, polynucleotides, and small organic molecules selectively inhibit PGHS-2. The court held that "[w]ithout such disclosure, the claimed methods cannot be said to have been described.").

It is noted that Applicants have claimed a large genus of immunostimulatory nucleic acids set forth in the claims, without sufficient structure of the immuno-stimulatory nucleic acid molecule. The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice (see i)(A), above), reduction to drawings (see i)(B), above), or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics,

sufficient to show the applicant was in possession of the claimed genus (see i)(C), above). See Eli Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406.

A "representative number of species" means that the species, which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. The disclosure of only one species encompassed within a genus adequately describes a claim directed to that genus only if the disclosure "indicates that the patentee has invented species sufficient to constitute the gen[us]." See Enzo Biochem, 323 F.3d at 966, 63 USPQ2d at 1615; Noelle v. Lederman, 355 F.3d 1343, 1350, 69 USPQ2d 1508, 1514 (Fed. Cir. 2004) (Fed. Cir: 2004)("[A] patentee of a biotechnological invention cannot necessarily claim a genus after only describing a limited number of species because there may be unpredictability in the results obtained from species other than those specifically enumerated."). "A patentee will not be deemed to have invented species sufficient to constitute the genus by virtue of having disclosed a single species when ... the evidence indicates ordinary artisans could not predict the operability in the invention of any species other than the one disclosed." In re Curtis, 354 F.3d 1347, 1358, 69 USPQ2d 1274, 1282 (Fed. Cir. 2004)(Claims directed to PTFE dental floss with a friction-enhancing coating were not supported by a disclosure of a microcrystalline wax coating where there was no evidence in the disclosure or anywhere else in the record showing applicant conveyed that any other coating was suitable for a PTFE dental floss.) On the other hand, there may be situations where one species adequately supports a genus. See, e.g., Rasmussen, 650 F.2d at 1214, 211 USPQ at 326-27 (disclosure of a single method of adheringly applying one layer to another was sufficient to support a generic claim

to "adheringly applying" because one skilled in the art reading the specification would understand that it is unimportant how the layers are adhered, so long as they are adhered); In re Herschler, 591 F.2d 693, 697, 200 USPQ 711,714 (CCPA 1979) (disclosure of corticosteroid in DMSO sufficient to support claims drawn to a method of using a mixture of a "physiologically active steroid" and DMSO because "use of known chemical compounds in a manner auxiliary to the invention must have a corresponding written description only so specific as to lead one having ordinary skill in the art to that class of compounds. Occasionally, a functional recitation of those known compounds in the specification may be sufficient as that description."); In re Smythe, 480 F.2d 1376, 1383, 178 USPQ 279, 285 (CCPA 1973) (the phrase "air or other gas which is inert to the liquid" was sufficient to support a claim to "inert fluid media" because the description of the properties and functions of the air or other gas segmentizing medium would suggest to a person skilled in the art that appellant's invention includes the use of "inert fluid" broadly.).

10. Claims 1, 64, 66, 67, 69-75, 77-81, 83-85, 89 and 91 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The pending claims (for example claim 1) are a method for inducing an immune response comprising topically administering to a subject an oil-water emulsion and an immunostimulatory nucleic acid in an amount effective to induce an immune response. Claim 64 defines the nucleic acid as a CpG

immunostimulatory nucleic acid. The species elected was herpes simplex virus infection.

It is noted that the preamble of the independent claim, claim 1, does not recite if this immune response is being induced in a subject or a test tube; it is not clear if Applicants intend *in vitro* or *in vivo* methods.

A review of the specification discloses a list of immunostimulatory nucleic acids that could be used in the claimed invention. However, they comprise 8 or more nucleic acids (see for example Table 1) not the 2 nucleic acids (C, G) as set forth in claim 64 and there is no structure set forth in independent claim 1.

The state of the art is unpredictable with regard to the use of oligonucleotides of less than 8 nucleotides having immunostimulatory activity. Yamamoto et al 1994 (Antisense Research and Development, 1994, 4:119-122) teaches that "immunostimulatory activity of oligonucleotides 18 bases or more in length was observed and was proportional to the base length, with a maximum at 22-30 bases. On the other hand, the oligonucleotides 16 bases or less in length were not as active even if they possessed the palindromic sequences. These results indicate that the immunostimulatory activity of oligonucleotides with certain palindromic sequences requires an oligonucleotide at least 18 bases long." (abstract).

The state of the art is unpredictable with regard to treatments using CpG. CpG containing oligonucleotides are currently being investigated for exerting their immunotherapeutic effects in various organisms (See Krieg et al, Weiner and McCluskie et al for recent advances using CpG oligonucleotides). Biological responses to the administration of CpG containing oligonucleotides vary, however, depending on the mode of administration and the organism (See McCluskie et al in

its entirety, and especially on page 296; see Krieg et al on page 524). Weiner states furthermore that the molecular mechanisms of CpG oligonucleotides' immuno-stimulatory effects are not yet understood (See especially page 461). Further, Weiner cautions that despite therapeutic promise of some CpG ODNs, all CpG ODNs are not alike and more needs to be learned about the heterogeneous responses that occur based on host organism, cell subset or CpG ODN sequence. Weiner teaches that the clinical effects of CpG ODN have not yet been explored and further work with the immunostimulatory nucleic acids in both the laboratory and the clinic are needed before their true promise as investigational immuno-logical and therapeutic agents is known.

In view of all of the above it would require undue experimentation to practice the claimed invention. Factors to be considered in determining whether undue experimentation is required, are set forth in In re Wands 8 USPQ2d 1400. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and (8) the breadth of the claims.

Applying the above test to the facts of record, it is determined that 1) no declaration under 37 C.F.R. 1.132 or other relevant evidence has been made of record establishing the amount of experimentation necessary, 2) insufficient direction or guidance is presented in the specification with respect to a method of inducing an immune response in a subject comprising administering an immunostimulatory nucleic acid comprising only a C, G, or one having no defined structure, 3) the relative skill of those in the art is commonly recognized as quite

high (post-doctoral level). With regard to (4) the nature of the invention and (5) the state of the prior art, these have been discussed above. One of skill in the art would require guidance, in order to make or use the method and immuno-stimulatory nucleic acids as claimed. The claims are enabled for SEQ ID NO: 150 and a method of administering SEQ ID NO: 150 as set forth in the instant specification. For reasons stated above (i.e. lack of enabling disclosure, unpredictability of the art, lack of guidance) it would require undue experimentation to practice the claimed invention. A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. In re Wright, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993). In view of all of the above, the pending specification does not enable the claimed invention and therefore the pending claims are not enabled.

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

12. Claims 1, 64, 66, 67, 69, 71-73, 77-81, 83-85 are rejected under 35 U.S.C. 102(b) as being anticipated by Cohen et al (WO 01/00231 A2, publication date January 4, 2001).

Cohen et al discloses a composition comprising an immunostimulatory nucleic acid and oil-in-water emulsion and a method of inducing an immune response in a subject (abstract; p. 8; claims). Cohen et al discloses the phosphate backbone modifications (p. 6). The prior art anticipates the claimed invention.

13. Claims 1, 64, 66, 67, 69-75, 77-81, 83-85 and 91 are rejected under 35 U.S.C. 102(e) as being anticipated by Babiuk et al (US 2005/0238660 A1 filing date October 7, 2002).

Babiuk et al discloses invention involves methods and compositions of an immunostimulatory nucleic acid in combination with other therapeutic formulations such as oil-in-water emulsions. The combination of therapeutics are administered in various dosages or at various time schedules for the treatment of disorders such as disease and cancer (abstract; claims).

[0007] In one aspect the invention relates to a method for reducing viral shedding in a non-human animal by administering to a non-human animal infected with a virus or at risk of viral infection, an immunostimulatory nucleic acid and an oil-in-water emulsion in an effective amount to reduce viral shedding. In one embodiment the oil-in-water emulsion is EMULSIGEN.TM. Optionally the non-human animal is a dog, cat, horse, cow, pig, sheep, goat, primate or chicken.

[0008] The combination of active agents may be administered with or without an antigen or an antiviral agent. In some embodiments the antiviral agent is selected from the group consisting of Acemannan; Acyclovir, Acyclovir

Sodium; Adefovir; Alovudine; Alvircept Sudotox; Amantadine Hydrochloride; Aranotin; Arildone; Atevirdine Mesylate; Avridine; Cidofovir; Cipamfylline; Cytarabine Hydrochloride; Delavirdine Mesylate; Desciclovir; Didanosine; Disoxaril; Edoxudine; Enviradene; Enviroxime; Famciclovir; Famotine Hydrochloride; Fiacitabine; Fialuridine; Fosarilate; Foscarnet Sodium; Fosfonet Sodium; Ganciclovir; Ganciclovir Sodium; Idoxuridine; Kethoxal; Lamivudine; Lobucavir; Memotine Hydrochloride; Methisazone; Nevirapine; Penciclovir; Pirodavir; Ribavirin; Rimantadane Hydrochloride; Saquinavir Mesylate; Somantadine Hydrochloride; Sorivudine; Statolon; Stavudine; Tilorone Hydrochloride; Trifluridine; Valacyclovir Hydrochloride; Vidarabine; Vidarabine Phosphate; Vidarabine Sodium Phosphate; Viroxime; Zalcitabine; Zidovudine; and Zinviroxime.

[0010] According to other aspects the invention is a method for inducing an immune response by administering to a subject an oil-in-water emulsion and a CpG oligonucleotide in an effective amount to produce the immune response. Optionally the immune response is an antigen specific immune response and the subject is administered an antigen. In one embodiment the oil-in-water emulsion is EMULSIGEN.TM..

[0014] The immunostimulatory nucleic acid, such as the CpG oligonucleotide may be administered by any route. For instance the immunostimulatory nucleic acid may be administered orally, by injection, or through a sustained release device.

[0015] In some embodiments of the invention the subject has a cancer or an infectious disease. In other embodiments the subject is at risk of developing a

cancer or an infectious disease. Optionally the subject has a cancer selected from the group consisting of bone cancer, brain and CNS cancer, connective tissue cancer, esophageal cancer, eye cancer, Hodgkin's lymphoma, larynx cancer, oral cavity cancer, skin cancer, and testicular cancer. The subject may also be an immunocompromised subject. In other embodiments the subject has an infectious disease selected from the group consisting of a viral bacterial, fungal and parasitic infection In yet another embodiment the subject is at risk of developing an infectious disease elected from the group consisting of a viral, bacterial, fungal and parasitic infection. See also [0041], [0043], [0047]

[0016] The immunostimulatory nucleic acid may have a modified backbone, such as a phosphate modified backbone or a peptide modified oligonucleotide backbone. In one embodiment the phosphate modified backbone is a phosphoro-thioate modified backbone. See also [0095]; [0114]; [0115]; [0116]

[0017] In other aspects the invention is a composition of an immuno-stimulatory nucleic acid and an oil-in-water emulsion. In one embodiment the oil-in-water emulsion is EMULSIGEN.TM..

[0018] In certain embodiments of all aspects of the invention, the immunostimulatory nucleic acid may be a nucleic acid which stimulates a Th1 immune response. Similarly, in some aspects of the invention, it is conceivable that one or more different immunostimulatory nucleic acids may be administered to a subject. Thus depending on the embodiment, one, two, three, four, five or more different immunostimulatory-nucleic acids may be administered to a subject in a particular method. Thus, the term "an immunostimulatory nucleic acid" is meant to embrace a single immunostimulatory nucleic acid, a plurality of

immunostimulatory nucleic acids of a particular class and a plurality of immunostimulatory nucleic acids of different classes.

[0019] According to other embodiments, the immunostimulatory nucleic acid is administered concurrently with, prior to, or following the administration of the other therapeutic formulation, e.g., oil-in-water emulsion, antigen etc.

[0150] Immunostimulatory nucleic acid and therapeutic formulation may be administered by any ordinary route for administering medications. Depending upon the type of disorder to be treated, immunostimulatory nucleic acids and therapeutic formulations may be inhaled, ingested or administered by systemic routes. Systemic routes include oral and parenteral. Inhaled medications are preferred in some embodiments because of the direct delivery to the lung, particularly in the treatment of respiratory disease or lung cancer. Several types of metered dose inhalers are regularly used for administration by inhalation. These types of devices include metered dose inhalers (MDI), breath-actuated MDI, dry powder inhaler (DPI), spacer/holding chambers in combination with MDI, and nebulizers. Preferred routes of administration include but are not limited to oral, parenteral, intramuscular, intranasal, intratracheal, intrathecal, intravenous, inhalation, ocular, vaginal, and rectal.

[0151] For use in therapy, an effective amount of the immunostimulatory nucleic acid and therapeutic formulation can be administered to a subject by any mode that delivers the nucleic acid to the affected organ or tissue, or alternatively to the immune system. "Administering" the pharmaceutical composition of the present invention may be accomplished by any means known to the skilled artist. Preferred routes of administration include but are not limited to oral, parenteral,

intramuscular, subcutaneous, intranasal, intratracheal, inhalation, ocular, vaginal, and rectal.

[0096] In some embodiments, a CpG immunostimulatory nucleic acid is used in the methods of the invention. A CpG immunostimulatory nucleic acid is a nucleic acid which contains a CG dinucleotide, the C residue of which is unmethylated. CpG immunostimulatory nucleic acids are known to stimulate Th1-type immune responses. CpG sequences, while relatively rare in human DNA are commonly found in the DNA of infectious organisms such as bacteria. The human immune system has apparently evolved to recognize CpG sequences as an early warning sign of infection and to initiate an immediate and powerful immune response against invading pathogens without causing adverse reactions frequently seen with other immune stimulatory agents. Thus CpG containing nucleic acids, relying on this innate immune defense mechanism can utilize a unique and natural pathway for immune therapy.

The prior art anticipates the claimed invention.

14. Claim 82 is objected to because it depends from rejected claim 1.

15. No claims are allowed.

16. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to N. M. Minnifield whose telephone number is

571-272-0860. The examiner can normally be reached on M-F (8:00-5:30) Second Friday Off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shanon Foley can be reached on 571-272-8975. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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/N. M. Minnifield/
Primary Examiner,
Art Unit 1645